REMARKS

Reconsideration of the allowability of the present application is requested respectfully.

Status of the Claims

Claims 1 to 31 were acted upon by the Examiner in the Office Action dated August 11, 2004. Claims 1 to 31 have been rejected. Claims 1 and 25 have been amended. No claims have been cancelled. No Claims have been added. Accordingly, Claims 1 to 31 are presented for examination.

Support for Amendments

Claim 25 has been amended to recite "A method for preparing a stabilized recombinant adenovirus vector formulation comprising preparing an admixture of a recombinant adenovirus vector comprising ...". Support for this amendment is found on 15, lines 2 to 5, of the application. Both claims 1 and 25 have been amended to delete reference to enhancing a titer.

ARGUMENTS

The 35 U.S.C. §102(a) Rejections

Claims 1 to 6, 22, and 23 to 28 have been rejected under 35 U.S.C. §102(a) as being anticipated by Crespo et al. (WO 97/33975, wherein the English version is US 6,248,588).

Applicants respectfully traverse the rejection.

Claim 25 has been amended to recite "A method for preparing a stabilized recombinant adenovirus vector formulation comprising preparing an admixture of a recombinant adenovirus vector comprising ...". Accordingly, all of the pending claims are directed to compositions comprising adenoviral vectors or methods of preparing adenoviral vector formulations.

Crespo et al. discloses medium for the cryopreservation of "biological materials". Column 6, lines 58 to 60, of Crespo et al. recites:

> Biological material is generally understood to mean any material containing a genetic information, which is self-reproducible or reproducible in a biological system. The said biological material may consist more particularly of cells or viral particles or both. Among the cells which may be frozen, there may be mentioned, for example, blood cells, bone marrow cells, cells producing viral particles ("packaging" lines), or genetically modified cells.

Column 6, line 66, to column 9, line 52, further discloses different types of viral particles and cell lines that qualify as "biological material". Crespo et al. does not describe vectors or any type of polynucleotide as "biological material".

The Examiner has asserted that Crespo et al. discloses "...that the composition can be used for storage, thawing and subsequently for a direct injection of the adenoviral vectors in a subject, whereby the adenoviral vectors are free of contaminants and toxic agents, and thus, are stabilized in performing their intended biological function, e.g., delivery and expression of a gene product of choice." (Page 4, lines 13 to 17 of the present action). This is incorrect. Crespo et al. discloses

direct injection of cells and viral particles. Column 9, lines 53 to 57, of Crespo et al. recites:

> The use of a medium according to the invention makes it possible to preserve these cells and to inject them directly into an organism, without a centrifugation or washing stage, with a good viability and without affecting their capacity to produce therapeutic proteins or viruses, where appropriate.

In column 6, lines 58 to 60, Crespo et al. recites, "Biological material is generally understood to mean any material containing a genetic information, which is self-reproducible or reproducible in a biological system." While it could be argued that an adenoviral vector qualifies as containing genetic information that is reproducible in a biological system. Crespo et al. never explicitly states that biological material includes vectors, DNA, RNA, nucleic acids, oligonucleotides, antisense molecules, and the like. Crespo et al. only mentions biological material in regard to cells and viral particles.

Further support for the assertion that Crespo et al. does not disclose compositions comprising adenoviral vectors or methods of preparing adenoviral vector formulations is found in column 10, lines 26 to 28 of Crespo et al., which recites, "A medium according to the invention allows the freezing and thawing of biological material under conditions of high viability." Applicants submit that the terms "viability" or "viable" are terms that are never used to describe DNA, vectors, or nucleic acids. Accordingly, applicants submit that the medium/compositions of Crespo et al. are to be used for the preservation of cells and viral particles, not vectors or nucleic acids.

As the presently claimed invention is directed to compositions comprising adenoviral vectors or methods of preparing adenoviral vector formulations, and Crespo et al. does not disclose such compositions or methods, applicants respectfully

request that the rejection of claims 1 to 6, 22, and 23 to 28 under 35 U.S.C. §102(a) as being anticipated by Crespo et al. be withdrawn.

The 35 U.S.C. §103(a) Rejections

Claims 1, 6 to 17, 22 to 26, and 29 to 31 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Crespo et al. in view of Engler et al. (US 2003/0211598).

Engler et al. discloses buffers comprising a detergent or ethanol. Engler et al. has been cited for disclosure of Tris buffers. Crespo et al. has been cited based on the Examiner's assertion that Crespo discloses compositions for the preservation of adenoviral vectors. The Examiner asserts that the combination of Crespo et al. and Engler et al. render the presently claimed invention obvious.

Applicants respectfully traverse the rejection. With regard to a *prima facie* obviousness rejection the MPEP §2143 states:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.
>
> The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Accordingly, a proper *prima facie* case of obviousness requires three steps: 1) providing a suggestion or motivation to combine the references; 2) providing a reasonable expectation that the combination will be successful; and 3) providing a combination that teaches all of the claim limitations. Steps 1) and 2) must be found

in the prior art. Applicant submits that the Examiner has not satisfied any of these requirements.

For the reasons noted above, that Crespo et al. does not disclose compositions comprising adenoviral vectors or methods of preparing adenoviral vector formulations. The teachings of Engler et al. provide no basis to overcome the deficiencies of Crespo et al. Accordingly, the Examiner has not satisfied the third requirement of teaching or suggesting all the claim limitations.

Furthermore, even if Crespo et al. did disclose compositions for the preservation of adenoviral vectors applicants assert that one of ordinary skill in the art would not be motivated to combine the human serum albumin-containing buffers of Crespo et al. with the detergent/ethanol-containing buffers of Engler et al.

Detergents and ethanol are known denaturants of proteins. Accordingly, a combination of the buffers of Crespo et al. and the buffers of Engler et al. would result in the human serum albumin (HSA) of the Crespo et al. buffers to become denatured. While Crespo et al. discloses that HSA may come from many sources, no where in Crespo et al. is it disclosed that the HSA may be denatured. Accordingly, the Examiner has not satisfied the first requirement of providing a motivation, found within Crespo et al. and Engler et al., to combine a HSA-containing buffer with a denaturant-containing buffer.

In view of this denaturation of HSA, the Examiner has not satisfied the second requirement of providing reasonable expectation of success. Considering that the denaturants of Engler et al. will denature the HSA of Crespo et al., an expectation that such a combination would be successful is not reasonable.

Accordingly, the Examiner has not satisfied any of the requirements of a *prima facie* case of obviousness. As such, applicants respectfully request that the rejection of claims 1, 6 to 17, 22 to 26, and 29 to 31 under 35 U.S.C. §103(a) as being unpatentable over Crespo et al. in view of Engler et al. be withdrawn.

Claims 1 to 31 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Crespo et al. taken with Engler et al. and further in view of Rolland et al. (US 6,040,295) and Sene (WO 98/02522, wherein the English version is US 6,451,256).

Applicants respectfully traverse the rejection.

Rolland et al. discloses compositions and methods for enhancing the uptake of nucleic acids by cells or organisms. Sene discloses methods for preserving viral particles in aqueous solution.

The incompatibility of the teachings of Crespo et al. with Engler et al. is discussed above. Rolland et al. and Sene provide no basis to overcome these deficiencies. Accordingly, applicants respectfully request that the rejection of claims 1 to 31 under 35 U.S.C. §103(a) as being unpatentable over Crespo et al. taken with Engler et al. and further in view of Rolland et al. and Sene be withdrawn.

A favorable action on the merits is requested respectfully. A Petition for a one-month extension of time, from November 11, 2004 to December 13, 2004 (December 11 being a Saturday), is enclosed.

Respectfully submitted,

Jonathan M. Dermott, Ph.D.
Reg. No. 48,608

Synnestvedt & Lechner LLP
2600 Aramark Tower
1101 Market Street
Philadelphia, PA 19107-2950
Telephone - (215) 923-4466
Facsimile - (215) 923-2189